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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,765	05/11/2001	Qingyun Liu	20351P	8413

210 7590 12/17/2003

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,765	LIU ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 1-33 are pending. Claim 33 stands withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-32 are under consideration.

Response to Amendment

Applicant's arguments filed 9/5/2003 have been fully considered but they are persuasive in part for the reasons set forth below.

The Objection to the Specification has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues are set forth below.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-32 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The claimed invention is not supported by either a credible, specific and substantial asserted utility or a well

established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The rejection of record set forth that it is clear from the instant specification that the nucleic acid encoding the HG51 polypeptide has been assigned a function because of its similarity to known proteins (Specification at 18, line 11). However, given the unpredictability of the use of sequence to function methods of assigning protein function are prone to errors. Applicant argues that there is no such unpredictability in the current field of sequence-homology- based prediction of functions for proteins, and that one of skill in the art could improve the homology based assertions of utility by realizing and avoiding the pitfalls. However, in the previous Office action the Doerks et al. reference demonstrated the errors inherent in sequence-function methods of assigning protein function. Therefore, based upon the evidence presented in the Doerks, Brenner and Bork reference showing the errors inherent in sequence-function methods of assigning protein function, the a preponderance of the evidence demonstrates that the HG51 polynucleotide and polypeptide lack a well-established, specific and substantial utility.

Additionally, the rejection of record set forth that even if, *arguendo*, the nucleic acid encoding the HG51 protein is found to be a G-protein coupled receptor, it is an orphan receptor. Since the ligand to this receptor is unknown, the function of the protein is also unknown. Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the HG51 protein, therefore, there is no "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required.

Applicant argues that orphan GPCRS, including HG51, can be used as candidates for therapeutic targets for a drug discovery approach called reverse molecular pharmacology, citing the Stadel reference. However, Stadel et al. teaches that the initial challenge is to determine the function of each orphan receptor through the identification of activating ligands and, once the function is clarified, link the orphan receptor to a specific disease and thus establish it as a candidate for a comprehensive drug discovery effort (page 433, column 1, first paragraph). Thus Stadel et al. teaches that before an orphan GPCR has a use, the activating ligand must be determined. Thus, without a known ligand, orphan receptors do not have a well-established, specific or substantial utility.

Applicant argues that the encoded polypeptide can be used in methods of drug discovery. However, the first requirement is that one must know the biological significance of the polypeptide that is being evaluated. Without this information, the results of the binding assay is useless because one would not know if the polypeptide activity should be increased or decreased or even what significance could be attributed to such changes in activity, or if the polypeptide has any function.

Applicant further argues that the encoded polypeptide can be used in diagnostic assays. However, in order for a polypeptide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to

know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polypeptide and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself.

Claims 1-32 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The rejection of record set forth that even if, *arguendo*, the HG51 polynucleotide and polypeptides are found to have a patentable utility, claims 26-32 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying an agonist or antagonist which binds SEQ ID NO: 2, or a substance which binds SEQ ID NO: 2, does not reasonably provide enablement for a method of identifying an agonist or antagonist which binds HG51, or a method of identifying a substance which binds HG51. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to practice the invention commensurate in scope with these claims, for reasons of record set forth in the Office Action of 6/3/2003. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

The rejection of record set forth that in the instant case, the claims are directed to a method of identifying an agonist or antagonist which binds HG51, or a method of identifying a substance which binds HG51. The specification discloses that the encoded HG51 polypeptide encompasses fragments, and mutants, including amino acid substitutions, deletions, additions and truncations (see specification at 5, lines 15-20). Thus, the claims encompass methods using variant proteins. Applicant has only taught SEQ ID NO: 1, encoding SEQ ID NO: 2. Applicant argues that the claims are drawn to "HG51" polypeptides not "biologically active fragments and/or mutant of HG51". However, the definition of the term "HG51" set forth in the Specification encompasses fragments, and mutants, including amino acid substitutions, deletions, additions and truncations, as shown *supra*. Thus, according to the definition of the term used, i.e. HG51, the claims encompass methods using variant polypeptides, and given the breadth of claims 26-32 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Claims 26-32 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 6/3/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a method of identifying an agonist or antagonist which binds HG51, or a method of identifying a substance which binds HG51. The specification discloses that the encoded HG51 polypeptide encompasses fragments, and mutants, including amino acid substitutions, deletions, additions and truncations (see specification at 5, lines 15-20). Thus, the claims encompass methods using variant proteins. Applicant has only taught SEQ ID NO: 1, encoding SEQ ID NO: 2.

Applicant argues that the claims are drawn to "HG51" polypeptides not "biologically active fragments and/or mutant of HG51". However, the definition of the term "HG51" set forth in the Specification encompasses fragments, and mutants, including amino acid substitutions, deletions, additions and truncations, as shown *supra*. Thus, according to the definition of the term used, i.e. HG51, the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 6-8, 17-19 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for in vivo transfection, for reasons of record set forth in the Office Action of 6/3/2003.

The specification on page 22 discloses that the nucleic acids of the current invention can be expressed in a wide variety of host cell types, including cells within a host animal. However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a DNA sequence as set forth in SEQ ID NO: 1 in an animal. Applicant argues that one of skill in the art would know that the expression of a recombinant protein in cells within a host animal can also be achieved with approaches other than gene therapy, such as the techniques of transgenic animals. The reference cited in the previous action established that numerous factors complicate *in vivo* gene expression which have not been shown to be overcome by routine experimentation. The claims as written are not limited to either host cells in culture, or transgenic animals, but encompass in vivo gene expression. Since the Specification does not set forth methods to enable one of skill in the art to make and use such host cells, the claims as written are not fully enabled.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-32 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record set forth in the Office Action of 6/3/2003.

Claim 25 is vague and indefinite in the recitation of the term "effect". There is no guidance provided in the claim as to what effect is to be measured, therefore the metes and bounds of the claim cannot be determined. Applicant argues that the "effect" is set forth in the Specification. However, it is not clear whether the effect of the test substance is to inhibit binding of a ligand, to alter possible second messenger transduction, or to modulate the expression of the encoding mRNA, thus the metes and bounds of the claim cannot be determined.

Claim 26 is vague and indefinite due to the recitation of the term "potential". It is not clear whether the claim is directed to a method of finding an agonist or antagonist, or whether it is directed to finding substances that, upon further chemical modifications could serve as agonists or antagonists. Applicant argues that the term "potential" is indicative of further method steps, which are not set forth, which are needed to verify the status of the test compound as an agonist or antagonist. The claim is thus incomplete for omitting essential steps, according to Applicant's argument, and such omission amounts to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps necessary to determine the status of the test compound as an agonist or antagonist.

Claim 26-32 are vague and indefinite in the recitation of the terms "HG51". There is no definition within the claim to define the protein to which this acronym refers. Thus, the metes and bounds of these claims cannot be determined. Applicant argues that the term HG51 is

limited to the amino acid set forth in SEQ ID NO: 2. However, the specification discloses that the encoded HG51 polypeptide encompasses fragments, and mutants, including amino acid substitutions, deletions, additions and truncations (see specification at 5, lines 15-20). The metes and bounds of the claims thus cannot be determined.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 2, 2003

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